UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,057	02/26/2002	Antoine F Carpentier	249326USOX PCT	4658

22850 7590 01/02/2009

OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
01/02/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	09/937,057	CARPENTIER, ANTOINE F	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *89-92,94-100,102 and 103* is/are allowed.

6)☒ Claim(s) *93,101 and 104-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communications filed 11-6-08.

Claims 89-107 are pending in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11-6-08 has been entered.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 101 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is being drawn to a composition comprising a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9, and further comprising a polymer.

The specification, claims and the art do not adequately describe the distinguishing features or attributes concisely shared by the members of the genus comprising *polymers*.

The specification teaches various cell delivery compositions, including colloidal dispersions and encapsulating agents. The examples provided at the time of filing, therefore, are not representative or correlative of the genus comprising *polymers*. Concise structural features that could distinguish structures within this genus (e.g., Which members of the genus, *polymer*, are useful for cell or tissue delivery?) from others are missing from the disclosure. (*e.g.*, What is encompassed by the term polymer that provides utility for the instant claims?). No common structural attributes identify the members of the claimed genus, and distinguish members within the genus from those outside of the claimed genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus claimed. Thus, Applicant was not in possession of the genus.

Claims 93, 104-107 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for tumor treatment following direct administration of a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9, does not reasonably provide enablement for the treatment of any cancer comprising any route of administration of a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to methods of treating any cancer comprising any route of administration of a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9.

The state of the prior art and the predictability or unpredictability of the art. Branch and Crooke teach that the in vivo (whole organism) application of molecules is a highly unpredictable endeavor due to target accessibility and delivery issues. Crooke also points out that cell culture examples are generally not predictive of *in vivo* inhibition of target molecules. (See entire text of A. Branch, Trends in Biochem. Sci., 23, 45-50, 1998; and S. Crooke, Ann. Rev. Med., Vol. 55, pages 61-95, 2004, esp. pages 71-72, 74, 81, 84-85).

Peracchi cites stability and delivery obstacles that need to be overcome in achieving desired in vivo efficacy: "A crucial limit of ribozymes in particular, and of oligonucleotide-based drugs in general, lies in their intrinsically low ability to cross biological membranes, and therefore to enter the cells where they are supposed to operate…cellular uptake following systemic administration appears to require more sophisticated formulations… the establishment of delivery systems that mediate efficient cellular uptake and sustained release… remains one of the major hurdles in the field." (See Peracchi et al, Rev. Med. Virol., 14, pages 47-64, 2004, abstract on page 47 and text on page 51).

Cellular uptake by appropriate target cells is a rate limiting step that has yet to be overcome in achieving predictable clinical efficacy. Both Chirila et al and Agrawal et al point to the current limitations which exist in our understanding of the cellular uptake of small molecules in vitro and in vivo (see Agrawal et al, Molecular Med. Today, Vol. 6, pages 72-81, 2000, especially at pages 79-80; see Chirila et al, Biomaterials, Vol. 23, pages 321-342, 2002, especially pages 326-327 for a general review of the important and inordinately difficult challenges of the delivery of therapeutic molecules to target cells).

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. The specification teaches the treatment of tumors in a subject comprising the direct intra-tumoral administration of SEQ ID No. 9. The specification fails to teach tumor reduction comprising the systemic administration of SEQ ID NO. 9. One skilled in the art would not accept on its face the

examples given in the specification of direct administration and subsequent treatment effects on that tumor as being correlative or representative of the ability to provide for the treatment of all cancers in a subject comprising the systemic administration of SEQ ID NO. 9, or of any a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT. There is a lack of guidance in the specification and an unpredictability associated with the successful targeting and delivery of therapeutic oligonucleotides to appropriate target cells in an organism to provide the treatment effects broadly claimed.

The breadth of the claims and the quantity of experimentation required. The claims are drawn to methods of treating any cancer comprising any route of administration of a stabilized oligonucleotide containing at least one nonmethylated octameric CG motif of the sequence AACGTTAT, nucleotides 9-16 of SEQ ID NO. 9, including the treatment of glioblastoma, medulloblastoma, neuroblastoma, melanoma or carcinoma. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of treatment effects for these cancers, including those requiring delivery of the therapeutic oligonucleotide through the blood brain barrier, or comprising administration other than direct intra-tumoral administration. Since the specification fails to provide sufficient guidance for the full scope claimed, and since determination of these factors is highly unpredictable, it would require undue experimentation to practice the invention over the full scope claimed.

Allowable Subject Matter

Claims 89-92, 94-100, 102 and 103 appear free of the prior art searched and of record.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz, can be reached on (571) 272-0763. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
12-17-08

/Jane Zara/

Primary Examiner, Art Unit 1635